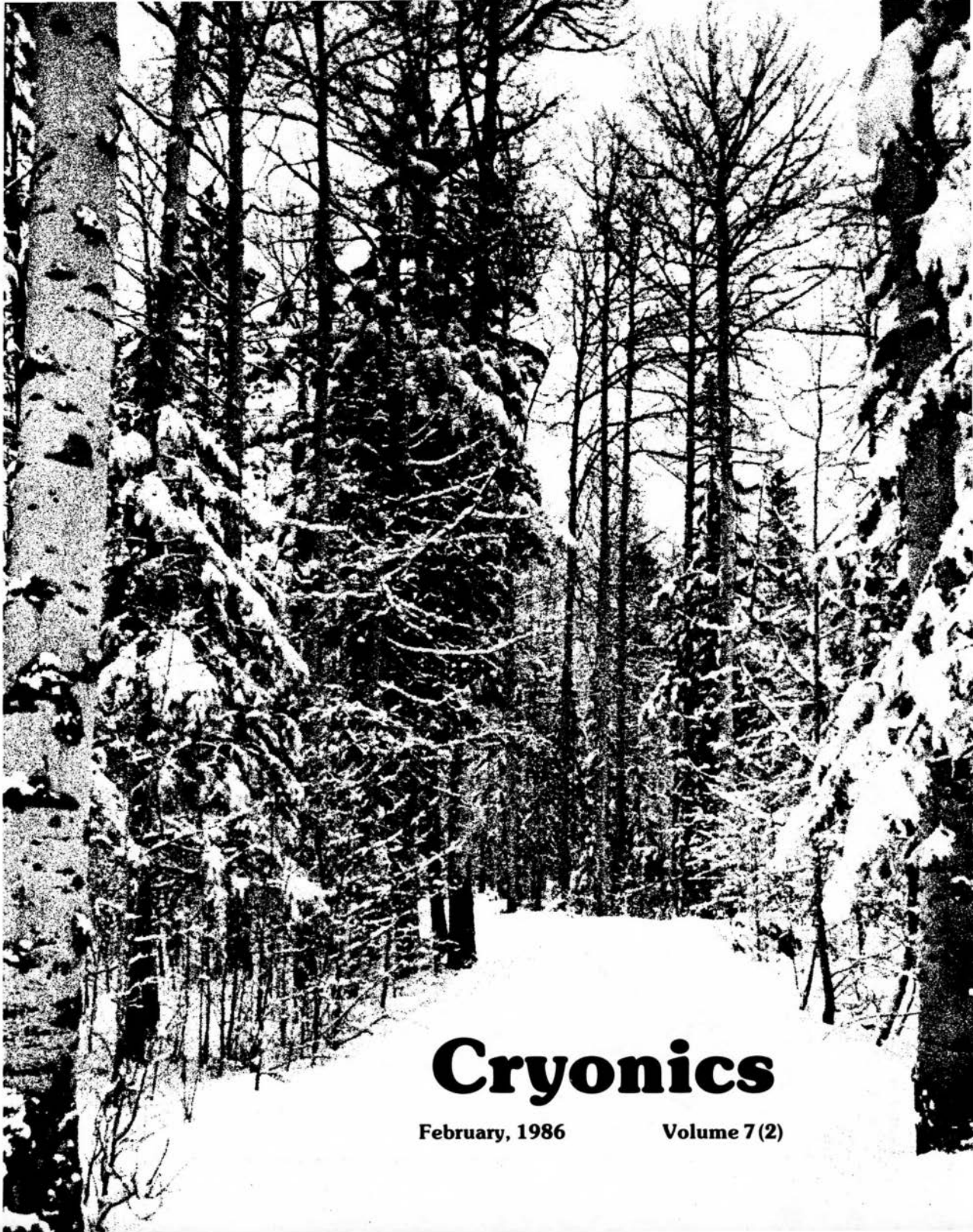
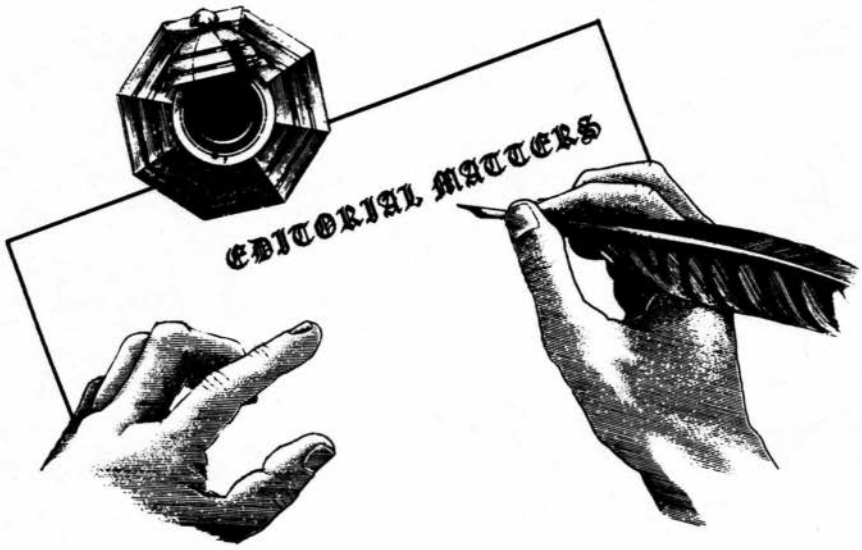


Cryonics

February, 1986 Volume 7 (2)

Volume 7(2) February, 1986 Issue#67

CRYONICS is the newsletter of the ALCOR Life Extension Foundation, Inc. Mike Darwin (Federowicz) and Hugh Hixon, Editors. Published monthly. Individual subscriptions: $15.00 per year in the U.S., Canada, and Mexico.; $30.00 per year all others. Group rates available upon request. Please address all editorial correspondence to ALCOR, 4030 N. Palm St., #304, Fullerton, CA 92635 or phone (714) 738-5569. The price of back issues is $2.00 each in the U.S., Canada, and Mexico, and $2.50 for all others.



ERRATA

In "Dixie's Rebirthday" on page 10 of the January issue, the Total Body Washout was done on December 8, 1984. An unusually large number of less serious bugs also crept into the text of the last issue, for which we apologize.

CRYONICS ON THE STANDS?

Now that our cover quality has improved, we've been giving some thought to putting the magazine in specialty bookstores (such as science fiction or libertarian bookstores). If you know of such outlets and would be interested in helping in this regard, let us know. Every little bit helps.

COORDINATOR UPDATE

We're now three-quarters of the way towards completing the first phase of providing equipment to Coordinators. The day after the December 8th ALCOR Turkey Roast, Fred and Linda Chamberlain came over to the ALCOR office and picked up their rescue kit. On December 29, our other two Northern California Coordinators, Thomas Donaldson and Cathy Woof, made the trip down from Silicon Valley and picked up 90% of their kit. Since they travelled by plane it was not possible to send the oxygen bottles back with them. Airline regulations completely forbid shipment of compressed gases and oxidizers under any circumstances. (As an aside, it is worth mentioning that if you require supplemental oxygen for medical reasons you cannot travel on commercial airlines. Period. In the past this has prevented or greatly delayed the transportation of terminally ill suspension patients who are remote from our facilities. Waiting until the last stages of illness before deciding to relocate is almost always a mistake!)

The situation with Cathy and Thomas' lack of oxygen bottles will be remedied in the near future since we will arrange to ship the bottles up by surface transportation. The problem with shipping oxygen is just one more example of why Coordinators are so potentially important. Oxygen is an item we cannot take with us in an emergency and which can be very difficult to get on short notice if you are not a resident of the area you are going into.

We still have one more kit to deploy and that is scheduled to go out to Indiana some time during the late spring or early summer of this year—finances permitting.

We will also be sending yet another Heart-Lung Resuscitator (HLR) out to Joe Cannon, a long time cryonics activist and ALCOR Suspension Member who lives some hours away from our facilities in South Florida. Joe has purchased an HLR and is in the process of making arrangements with a local ambulance company and hospital to stabilize him should the need arise. This is outstanding independent action on Joe's part and we hope to bring you the whole story of his efforts in the future. We should be shipping Joe's equipment to him sometime within the next two to three weeks.

ALCOR Coordinators Fred and Linda Chamberlain of Lake Tahoe.

GOLD BRACELETS AND QUALITY CONTROL

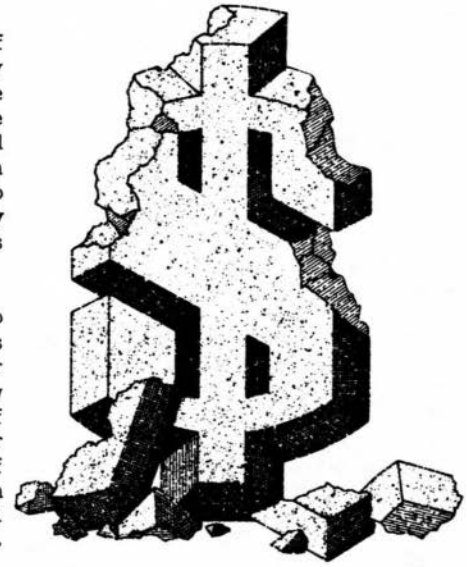
We have had a major problem with the second generation of gold filled ALCOR emergency ID bracelets. All of the second lot of bracelets we shipped were plated defectively and the gold literally rubs off with a few days of wear. We are both appalled and apologetic. It took a little detective work to figure out what was going wrong and why. Here's the story:

About 6 months ago we decided to offer gold filled bracelets and we began a testing program and offered half a dozen or so folks who attended one of our monthly meetings the opportunity to purchase bracelets at cost as "guinea pigs" to evaluate their durability and quality. This initial test went very well and we were more than satisfied with the vendor's performance. Subsequently, we plated several other batches, in particular a large batch just before Christmas! We do 100% inspection on almost everything that goes out of here (magazines are the only exception) and the bracelets looked great. What we didn't know was that the worker who did the actual work plating the bracelets failed to remove the chrome finish which is present on virtually all new stainless steel jewelry! (Incidentally, we weren't even aware that stainless steel jewelry is routinely given a thin chrome finish—to add luster!)

By the time many of the members who had ordered the bracelets received them, the gold was starting to come off—on the packaging, from the friction of

the chain, and so on. We had a lot of unhappy customers. Clearly, we had no way of knowing this was going to happen. We are sorry for the inconvenience and we would like to assure everyone who has had a problem that if they will simply return their bracelets we will rework them to their satisfaction **and refund the money they paid for them in full.** We feel it's the least we can do.

This is probably also a good time to point out that if you have **any** problems with the quality of any ALCOR goods or services you should let us know immediately. Sometimes we have no way of knowing something is wrong unless we hear about it from you. We want the quality of every aspect of our operation to remain high and that can only happen if **you** tell us what pleases as well as displeases you.



THE TIGHTROPE

by Mike Darwin and Jerry Leaf

Toward the back of this issue is the first half of a two part technical paper entitled "Case Report: Neuropreservation of ALCOR Patient A-1068." A dry enough title, and indeed the article itself is highly technical. Unless you've a good medical/scientific background with a special bent for cryonics and cryobiology, it will probably put you to sleep. And yet, between the lines of dry prose is a human drama and a struggle for life. We've tried to cover that struggle in terms more comprehensible to the layman in a previous article (see the April, 1985 issue of CRYONICS). However, it is every bit as important to tell the story from the technical aspect as well.

We firmly believe that this patient received the highest quality, most sophisticated care of any patient who has yet been placed into suspension. We say this with confidence and with pride. But also with humility. There was a lot of discussion as to whether or not we should make a full disclosure of the technical and procedural details which constituted this patient's care. Should we be ruthlessly honest about the errors we made in this patient's care and in the inherent limitations of the best of existing technology?

"A terrible question to ask," you are probably saying. We would agree and add "a terrible question to have to ask." Cryonics is in its infancy. And it has been, is, and will continue to be a troubled infancy. Why? Because cryonics suffers from the problem of deficient feedback. It is a serious problem, and one for which we have, as yet, no perfect solution. The problem can easily be illustrated by hard examples, examples which have led some cryonicists to question the wisdom of complete technical and patient care disclosure.

Some years ago, a man was placed into suspension by another cryonics organization using the best available techniques of the time. There were errors made (all of them **minor**, and inconsequential to the patient's care) and there were serious limitations on what was possible under the circumstances. The case was a last minute one, the cryonics organization involved was 3,000 miles away and it had just put together a new suspension team; a team which had not even had its first training session. Still, it is important to keep in mind that at that time that company was the **only** one that could deliver any kind of reasonable service, or would even have been willing to take the case under those conditions.

Cryovita Laboratories (where the suspension reported on here was carried out) was responsible for the perfusion and freezing of that patient. Jerry Leaf, the team leader, responsibly and ethically published a complete and honest technical report on the care given that patient. Some months later, Robert Ettinger, **at a public meeting**, made statements in the presence of this patient's relatives calling into question the quality of care the patient had received and even speculating that the patient might have been better off if he had simply been promptly frozen rather than subjected to the delay entailed in shipping the patient to Southern California and carrying out a perfusion which was not successful in introducing large amounts of cryoprotective agent.

In our opinion, this was an unconscionable thing to do. It was a profound emotional shock to the relatives of that patient and in our opinion it began a cycle of gnawing doubt, worry, and fear which ended in the removal of that patient from suspension. The family was panic-stricken. Had they made a mistake? Had they paid all that money for inadequate, worthless, or even **injurious** treatment? How could they **know**? When Mike Darwin first came into contact with this family he was not associated with Cryovita Laboratories, ALCOR, or any other California cryonics organization. The family asked him, among others, if he thought their relative had been mishandled or received inadequate care? He did his best to honestly reassure them: the care was the best available then, and indeed they were lucky to have found **anyone** to take them under the circumstances (deanimation having already occurred, limited finances, distance, and so on).

Yet, there was no way he could really convince them. And there was no way they could really know. In any other situation they could have found out sooner or later, one way or another. If someone is in a nursing home, in prison, in a coma, or gets medical care which is thought suspect, it is always possible to investigate, to wait for feedback or go in after it. But how do you get feedback from a body that is submerged in liquid nitrogen? How do you know, really know, that what was done was **right** or even that it was done at all? There are no experts to call on, and the patient doesn't get better, make a recovery, die, or even complain. All you are left with in such a situation is gnawing doubt. Toward the end, this family was so consumed with doubt and worry that they even were questioning whether or not their relative was being stored in liquid nitrogen!

Finally, the family decided to sue (for a whole host of reasons, some only peripherally related to the perfusion). The ripples of that one careless and unjustified remark began to spread. Suspension team members who did their best and made tremendous sacrifices were put on the line with the possibility of

losing everything--their homes, their savings, and even their marriages. While the litigation came to naught, that little fiasco caused three very fine suspension team members to walk away. Seasoned crew who had participated in a number of suspensions and who in some cases had medical and technical backgrounds which were invaluable suddenly were afraid to be involved; all because we had been honest.

Mike Darwin had a similar experience. In 1973, at the age of 17 while merely a visitor at a cryonics society of which he was a member, he participated in his first cryonic suspension. It was a traumatic and yet a very useful experience. It was traumatic because the conditions under which it was carried out were inexcusably bad, and beneficial because many of the current improvements we now have came out of it. He, and the other "amateur" participant in that suspension (who wishes to remain anonymous), took a rather unpopular stance at the time. They wrote up their findings and experiences in a technical report (the first of its kind) documenting the care this patient was given. There were many pollyannas who said they should have just shut up about it. And yet, had they not done what they did, many of the subsequent advances that were made simply wouldn't have happened. People need to know before they can act. What's more, just the act of writing up such a report forces one's thoughts into order and exposes those thoughts to the light of critical and constructive review by others.

The price that was paid for their effort came over 8 years later when there was an attempt to involve them in litigation over unrelated aspects of this patient's care. All because their names appeared on a paper which was written as a service to that patient and to all who would come later--including ourselves.

The ALCOR suspension team is, in our estimation, the most skilled and dedicated cryonic suspension team in the world. But it is made up of volunteers who are, by all objective criteria, amateurs. It is important to keep in mind the limits imposed on us by resources and reality. We were fortunate that the errors we made in this patient's care did not result in any harm. We believe we are also very fortunate to have the kind of people and the kind of organization which puts honesty before political considerations. Such honesty goes a long way toward redressing the problem of lack of feedback we discussed earlier.

Despite the tremendous overall improvement in this patient's care (as compared to all previous suspensions) the state of the art (apart from any errors or procedural oversights) leaves much to be desired. This is painfully obvious from the details of the report. We can, we will, and we must continue to do our best. But that is not good enough. We must strive ever harder, not only to eliminate errors, but to improve the basic techniques of cryonic suspension. That is a responsibility we all share, and how well we shoulder it will determine to a great extent what our chances are when **our** turn comes.

This patient and her husband are outstanding people. Their courage, strength and decency cannot be communicated by any printed report, technical or otherwise. It is the hope of all the Directors of ALCOR that they will trust us, and rest secure in the knowledge that the care given was the very best available. There is no question in our minds that the immense amount of data gathered and the learning which resulted from this suspension will aid those who follow tremendously.

We will continue in our policy of full and honest disclosure. In the long run, that is the only path open to us and the only one with any chance of real success.

CONTRIBUTIONS

A major fraction of ALCOR's income is in the form of donations. Our steady income from dues and emergency responsibility charges is able to cover our day-to-day operations and our emergency system, but we make progress on the basis of your contributions. We rely heavily on such contributions to conduct research and to improve the quality of our operation. It also has the virtue, if you're making a contribution with an eye to the tax advantages, of effectively making the government support cryonics, which is a much better deal than you'll get from the IRS. So, if you're counting on a good year ahead, give us a call or drop us a line. We'd like to count on a year of good progress too!

NEW POLICY ON DUES

Imagine going to your employer on payday and finding nothing. No check, no explanation, nothing. Not a very pleasant experience? An outrage? Unthinkable? We agree. And yet, that's what happens to us every three months. Every quarter a small (but significant) percentage of our suspension members simply doesn't pay their dues. In fact, they don't pay their dues until we've gone to the trouble of sending out a registered letter notifying them we're about to cancel their suspension arrangements.

The analogy of an employer who doesn't pay his employees is an apt one. Last month we had almost $600 of overdue accounts receivable for dues--for services we've already provided. That works out to the printing bill for two issues of this magazine or for a year of emergency answering service coverage! Unfortunately, our printer and our emergency answering service are not going to be as understanding as we've been.

So, sadly we've had to adopt a uniform policy, and we intend to enforce it. Effective as of January 5th, a 60-day grace period will be allowed after quarterly or yearly invoicing. If the dues are not in our hands by the end of the 60-day grace period, a registered letter will be sent notifying the member that suspension coverage will terminate in two weeks. At that time a $10.00 late fee will be imposed and additional proof of insurance will be required. To illustrate, suppose a member who is billed $40 quarterly allows the 60-day grace period to pass without sending in his payment. He will receive a registered letter saying he must pay **$50** within two weeks **plus supply proof of insurance in force to keep his suspension coverage intact. Additionally,** if he responds within the two-week period and retains his coverage, he will be getting the bill for emergency responsibility for the **next** quarter two weeks later, for another $40.

Clearly, making a prompt payment upon receiving your bill is the easiest way to keep your coverage in force!

Board Member Brenda Peters

SILCOOL: OVER THE TOP!

We're over the top! Thanks largely to the efforts of ALCOR Director Brenda Peters we raised over $2500. This fundraiser was an unprecedented success! It took us almost 3 years to raise a similar amount of money for the Cephalarium Vault! There is little doubt in the minds of the ALCOR Directors that Brenda's efforts were largely responsible for the astounding return. Our thanks: thanks to both Brenda, and to the many people who generously contributed.

By the time you read this we should have taken delivery on the Silcool fluid and have the flammable alcohol safely disposed of.

LIFE EXTENSION PHYSICIAN

Over and over again we have heard the question: "Do you know of any reputable, licensed physician I can go to who can help with a life extension program and/or who would not be hostile to cryonics?" Until recently, we've had no good answers to that question, but that's changed now. Recently Dr. Ward Dean, M.D. retired from his position as physician to the crack antiterrorist and special missions unit known as the Delta Force. Dr. Dean's career as a military physician is matched by a long-standing interest and participation in life extension medicine. In fact, the reason Dr. Dean went to medical school was to eventually practice life extension medicine.

A few months ago he settled in Los Angeles and opened what is probably the world's first and only life extension medical practice. Dr. Dean has established a general practice which will focus exclusively on patients wishing to practice life extension techniques. We should point out that Dr. Dean will also see his life extension patients for their other health needs as well.

Several of the Directors of ALCOR have recently had the opportunity to meet with Dr. Dean, and we have been uniformly impressed with his knowledge and no-nonsense approach. Dr. Dean has established

a program of laboratory tests to evaluate biological age which will be available in conjunction with antiaging therapies such as Hydergine, L-Dopa, and other therapeutic agents aimed at slowing down the clock. Dr. Dean's is the only medical clinic in the country devoted to full time research and clinical application of potential life extension therapies. A unique aspect of his practice is the development of a series of aging measurement test batteries. Such testing allows for feedback and interpretation of the effectiveness of a given protocol for extending life-span.

We think Dr. Dean's approach is a sane and healthy alternative to the often wild and unmonitored experimentation being undertaken by many "life extenders." We are very impressed by Dr. Dean's thoughtfulness and aggressive clinical stance, as well as his willingness to cooperate fully with a cryonic suspension member's arrangements should the need arise.

If you are in need of a physician who is thoroughly knowledgeable about potential life extension therapies **and cryonics** you can contact Dr. Dean at:

Ward Dean, M.D.
Life Extension Research
8760 Sunset Boulevard
Los Angeles, California 90069
(213) 652-5731

BIG BREAKTHROUGH!

In the center of this issue you'll find a stunning, glossy, 12-page brochure advertising the Life Extension Foundation's upcoming Life Extension Breakthrough Conference which will be held May 1 - 4 at the Disneyland Hotel in Anaheim, California. This conference promises to be very exciting and to offer plenty of opportunities for experts in various fields to get together and share their knowledge with each other and with you. World-class researchers in aging, cryobiology, and life extension, as well as several key members of cryonics organizations, will speak on their work and discoveries.

We won't go on at length here describing the conference in detail. The Foundation's superb brochure does it far better than we can.

While your are in Southern California for the conference, consider visiting our facilities here in Fullerton, which is less than 10 miles away. Since we are not here all the time, you should call ahead for an appointment.

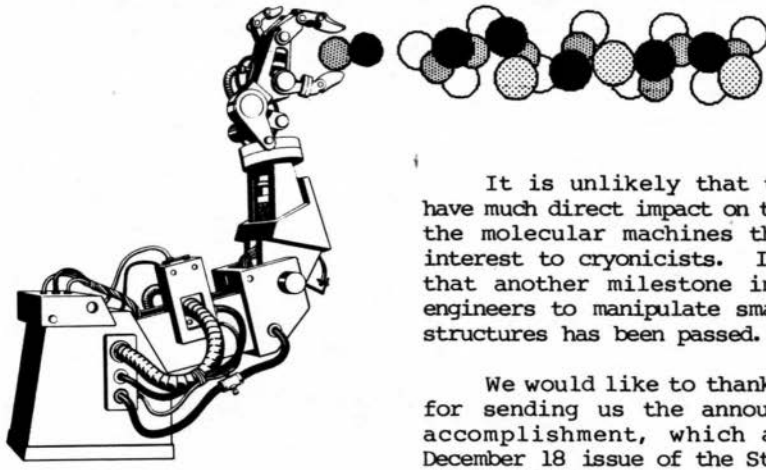
NANOWRITING: SECOND FEYNMAN PRIZE CLAIMED

In late 1959, Dr. Richard Feynman of Caltech offered two prizes of $1,000 each: for reducing a book page by a linear factor of 25,000 in such a manner that it could be read by an electron microscope; and for the construction of a rotating electric motor fitting inside a 1/64 inch cube. The prize for the motor was won in less than a year. Now, after 26 years, the prize for reducing a book page is being claimed by a student at Stanford University.

Tim Newman, a Stanford electrical engineering student, wrote the text of the first page of **A Tale of Two Cities** on a "page" 230 millionths of an inch square. To do so, he used a machine he designed to manufacture ultra-small electronic devices for research. The key component of the computer-controlled electron beam writer is an electron beam lens that allows the electron beam to be focused to a spot less than one millionth of an inch in diameter. The letter "i" in the text is about 50 to 60 atoms wide. To give you some idea of the density of information storage on this level we might add that it would be possible to put the information content of 22,500 such pages on the head of a pin! Imagine being able to carry around a library of 6,000 volumes on the average 9 mm contact lens!

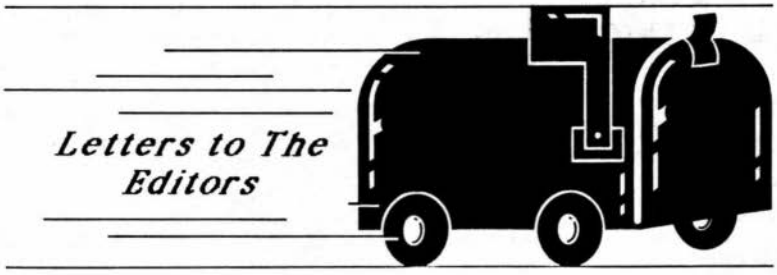
The text was written on a plastic film about one millionth of an inch thick. Bombardment of the plastic by the electron beam disrupts its molecular structure so that the plastic can be selectively etched away by a solvent. A transmission electron microscope is then used to read the text.

Newman's circuit writer was built as part of his research for a Ph.D. thesis. It was funded by the U.S. Army.



It is unlikely that this device will have much direct impact on the development of the molecular machines that are of great interest to cryonicists. It does illustrate that another milestone in the ability of engineers to manipulate smaller and smaller structures has been passed.

We would like to thank Frank Rothacker for sending us the announcement of this accomplishment, which appeared in the December 18 issue of the Stanford University **Campus Report.**



Dear Editors,

Thank you for the most interesting article **The Myth of the Golden Scalpel** in your January issue.

Since I wrote the words you quoted from my column in **The Immortalist** I have become aware of further facts about life in America which alter my views on the cost, to Americans, of cryonics.

One of these was a television programme **Whicker's World** about British expatriates living in the United States. He stated in the programme that whereas in Britain people appear to be proud of failure and are shameful of success, the opposite exists in the US. Therefore in America there may not be the jealousy between those that can afford cryonics and those that cannot.

I had previously thought that by not offering some hope to a large sector of the population, you may be risking that sector saying, "Well, if I can't have it, then no one else should." Obviously such people could pose a real threat to your operation.

However, I still feel that if there are ever to be cryonics facilities in the UK and a lot of other countries, it will be vital to those who are using the most expensive methods that there is some hope for the rest. Also, over a period of hundreds of years, it is possible that people in America may get "The British Disease" of abasement of financial success. I do not share your view that it would be immoral to offer some hope, however tenuous it is, especially if the differences are spelt out.

I have never felt that it would be correct for any of the immortalist organizations to do anything other than that which they themselves feel most appropriate. However I do think there is a case for some arrangement whereby a client can be switched to the most appropriate route at the time of death depending on the financial and physical circumstances of his death. I hope that ALCOR would not reject any more general immortalist organization wanting to offer its clients the option of an ALCOR contract, on the grounds that this other organization was offering peat bogs or whatever.

The other factor that has modified my views was an article in **The Financial Times** which placed the cost of an expensive funeral casket in California not far short of your neuropreservation option.

I think that your clients who opted for formaldehyde as opposed to neuropreservation could have been influenced by the thought that their suspendee

may wake up in the future, when the caring ideals of ALCOR are forgotten, as an animated head connected to a bench experiment only to endure a period of surgical torture before being exterminated once and for all. (As, for example, in C.S. Lewis' novel **That Hideous Strength.**)

The fact that all suspendees are legally dead and therefore have no rights makes this a matter of concern for many of the people to whom I have spoken on cryonics. If your **Reflecting Forward: ALCOR in 1985-6** article is correct in its prediction that you are near to substantially improved brain suspension, then possibly the day may come when people in suspension can be legally regarded as alive. The American Cryonics Society has commented that they have the best legal brains in cryonics on their team. Possibly this is a project they could pursue in cooperation with ALCOR.

When suspendees are legally alive, many of the difficulties presently experienced over autopsies, funding, and ownership of the body will go. Also the fear of experimentation will be reduced to that level experienced by any surgical patient.

John de Rivaz
Cornwall, England

To the Editors:

With regard to Mr. Schneiker's response to my letter criticizing his article **Prospects and Applications for the Genesis and Ultra Mass Production of Sub-Millimeter Machines, Devices, and Replicating Systems** (PAG), as Mr. Schneiker is aware, I disagree with his judgment regarding relative life-saving merits of different rates of development of nanotechnology. While I am generally a technophile, the prospect of a technology that would allow a hobbyist to build a weapons system capable of destroying the biosphere may legitimately inspire some caution, even if that technology also has great medical promise. I differ in my evaluation of the situation: the effects of having this capability loose in the world (particularly if we have not had time to prepare) do not strike me "as for practical purposes effectively nil" (to quote PAG). But then, I am not privy to knowledge of such "Current technologies of oppression . . . and destruction [as] . . . individual and global forms of secret recombinant-DNA-based, biochemical weapons with genetically selective or other targeting." Though I suspect that his proposed policies would increase the likelihood of the extinction of the human race, my understanding of his views and motives is such that I see no reason to describe him as "callous in the extreme." I wish he would extend the same understanding and courtesy regarding my own views and motives.

Regarding Mr. Schneiker's discussion of priority, "proposing cell repair machines" is an ambiguous term. I certainly cannot claim to have originated the idea of making small devices for repairing cells; my forthcoming book references the earlier suggestions. What I <u>did</u> do was to construct a tight argument for the feasibility of reaching cells, entering them, characterizing their contents, and processing the resulting information in a fairly well-defined sort of molecular computer, followed by the reworking of the cell's molecular and supramolecular structures under computer direction, the exit of the machines, and the startup of metabolism. This argument takes account of a wide range of constraints (ranging from computational to thermal) and includes the outlines of

a system-level design, based on my component-level work on mechanical nanocomputers.

Systems of this sort will allow the creation of essentially any desired biological state, so long as enough information exists to allow one to infer what state is in fact to be desired. This certainly allows the indefinite extension of life, and it almost certainly allows the recovery of a person from current suspension procedures. Unlike the editors of this magazine, Mr. Schneiker appears unaware of this work. This may excuse him on several points.

Mr. Schneiker suggests that I have not read Dr. Feynman's talk (referenced in the **Proceedings of the National Academy of Sciences**), and mentions "the biomolecules [Feynman] cites as examples of miniature machines." Perhaps we have read different transcripts, but my rereading of that talk fails to turn up any such discussion of biomolecules as miniature machines. It refers to biological phenomena as an inspiration, to cells as wiggling and walking, and to biomolecules as objects of study--but not to biomolecules as examples of machines. Dr. Feynman may very well have thought about it, but he didn't say it, and apparently didn't follow up on it in over twenty years.

If the literature contains a clear exposition of how universal assemblers can build molecular machines--one that predates my 1981 paper--then I have yet to hear of it. Dr. Feynman's 1959 talk comes closest, but after discussions of other matters, it basically says that "There's no physical reason why we can't synthesize any desired chemical substance by maneuvering atoms," rather than saying "Here's how we can build machines able to build arbitrarily complex systems to atomic specifications, and here's why we can be sure it will work." Further, I found out about Dr. Feynman's talk only after I began to write up my paper.

Mr. Schneiker also cites Dr. Feynman's talk in connection with priority on cell repair machines. This is grasping at straws to an extent that suggests a distinct bias: the only repair machine Dr. Feynman discusses is a mechanical heart-valve-surgeon several billion times bulkier than a cell repair machine—and lacking any onboard computer. Further, he attributes the idea to his friend, Albert R. Hibbs.

In an apparent effort to suggest that my paper in the PNAS was inadequately refereed, Mr. Schneiker notes that Dr. Feynman did not serve as a referee. In declining, Dr. Feynman stated that, as a matter of policy, he never referees papers. Noted physicists Phillip Morrison and Freeman Dyson did serve, and the paper has since been cited as a seminal work by molecular biologists writing in both **Science** and **Nature**. In any event, there is no need to "guarantee that the most qualified referees participate" when the goal is merely to reduce the amount of nonsense in circulation. Basic competence will often suffice.

But enough of responding to attacks. In my critique, I selected two of Mr. Schneiker's proposals to illustrate the technical errors found in PAG. His reply to these criticisms is instructive.

In response to the first--my criticism of his giant-blob-of-cells-to-design-tiny-devices proposal--he mentions the literature on "stochastic automata, analog associative memory, and randomly connected neural networks," but he fails to cite any work indicating how his "very simple, communicating, [and randomly connected] state machines" can be made to act as even an adding

machine, much less as an artificially-intelligent supercomputer. A glance at any anatomy text will show that the brain is not a randomly connected neural network—nor are neurons simple state machines.

Regarding my criticism of the sheer size of the proposed blob, he finds my comments on the state of the art in cell culture "amusing" in light of industrial-scale microbial fermentation. But this suggests that he has missed my point. Cells in a fermenter form a suspension, not a solid mass, hence the technologies are not comparable.

His belated proposal to include a vascular system in his mass of cells makes it clear that he is talking not about cell culture, but about the design, genetic engineering, and growth of a novel sort of organ—the size of a "large oil storage tank," no less. This is decidedly beyond the state of the art; when combined with our ignorance of how to make such a thing think, the idea of developing one in order to design factory-like molecular machines seems rather peculiar. His observation that we build complex computers to design simple devices also misses the point: since we know how to design and build computers, it makes sense to do so, and to use them for whatever they are good at. Eventually, using assembler-built instruments and components, we will learn to build brain-like devices--but as I said in my critique, not as a step toward building devices vastly simpler than the brain. Applications after development are another matter.

Mr. Schneiker mounts a strong offense on my second illustrative example. In critiquing his nanometer-scale dipoles, I had mentioned the frequency limits of present-day amplifiers. He seizes on this, and states that my "dismissal of nanometer scale antennas as 'wholly implausible on a variety of grounds' fails since you don't need amplifying circuits to drive antennas." He then suggests that my physics is "a bit weak." But a strong offense is not the same as a defense. He points to the rapid advance in the upper frequencies of circuits, and says that their present capabilities are irrelevant to ascertaining their ultimate capabilities. But I had mentioned present amplifiers merely for comparison. (And yes, it would have been better to substitute the word "oscillators.") Further, present capabilities aren't the point. Physics is. Naive extrapolation of advances in engine efficiency would suggest the possibility of engines with over 100% efficiency, violating the conservation of energy. There are limits to dipole antennas as well.

I refer to his nanometer-scale, quarter-wave dipoles as emitting (as they must) X-rays in the hundred electron volt range, and Mr. Schneiker does not object to this characterization. Very well: what are some of the 'various grounds' for considering this wholly implausible? For one, these X-rays must result from 100 eV excitations in the dipoles, but this is tens of times the energy needed to eject electrons from the metal. For a second, a single 100 eV photon is enough to raise the temperature of a cubic nanometer of material to something like 10,000°C. For a third, objects of this size, (that is, molecules) have characteristic emissions in the infrared or visible bands, not in the X-ray band. For a fourth, leaving aside processes involving high-energy particles, X-rays are emitted by the tightly-bound electrons of an atom's inner shells, not by the conduction electrons of a metal. For a fifth, (which addresses the plausibility of the requisite oscillator), the time required for an electron at the Fermi level to cross even a single atomic diameter is longer than the oscillation period of a 100 eV X-ray. A phased array of such dipoles, as proposed in PAG, is doubly ridiculous. If the phrasing of my original

critique left anyone else with the impression that my thinking about the limits of technology is guided by a simple-minded comparison with present practice, I hope this sets the record straight.

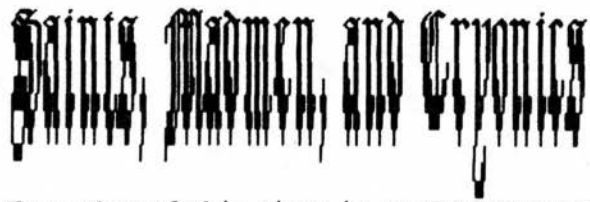
Mr. Schneiker claims that I had few critical comments regarding earlier drafts of his article (as I recall, my comments focused on a few general points and a few matters relating to the portrayal of my own work). He cites my remark, "Those are some references! Thanks." as evidence that I have since had a "radical change of opinion" regarding the quality of the material. But my recent critique noted that PAG is "rich in citations"; these citations are indeed impressive in quantity and often quite interesting, despite their omissions and lapses in quality (some of the papers cited contain nonsense). As for my failure to invest days in preparing a complete, detailed critique of this mass of material, the reader's imagination can perhaps supply an explanation that does not involve my having greatly admired its technical quality.

In closing, I note that my criticism of PAG has provoked a response that includes ad hominem attacks, references to things allegedly said at conferences, statements about what someone said he thought I said about trivial revisions to my book, and so on, and so forth. Despite this muddying of the debate, my criticisms of the technical content of PAG have not been effectively rebutted, and I will again assert (I hope with some credibility) that many more could be made.

Sensible readers now have enough information to judge matters, and so I will lay down my end of what would likely be an unproductive exchange. Readers wishing to know more about nanotechnology (including the key concepts of assemblers, disassemblers, nanocomputers, replicating assemblers, cell repair machines, active shields, and sealed assembler labs) may want to examine my book **Engines of Creation**, scheduled for publication this May by Doubleday.

K. Eric Drexler
Redwood City, CA

Editor's note: Thank you, Eric, for "laying down your end" of this exchange, and we will publish no further installments to this exchange by either you or Conrad Schneiker.



EDITOR'S NOTE: The author of this piece is an ALCOR Suspension Member who wishes, for reasons of privacy and confidentiality of medical records, to remain anonymous. We publish it without attribution because we feel it offers valuable insights and useful advice.

During discussions with noncryonicists about cryonics, a frequent statement which is made is that cryonics is "just another religion". I can only conclude that this is an effort to dismiss the idea by redefining it in familiar terms.

The hidden curriculum here is that it is "**just** a religion," that is, a system of **beliefs** about life and death.

I find this definition disturbing. I cannot see any connection. I have found it sufficiently disturbing for me to have taken the time to examine it from my own psychological perspective.

Religiously speaking, until the age of 19, I was a Presbyterian. Church most Sundays, Sunday school teacher, fellowship, bible camps—the whole baggage of conservative religious belief. An education in science, a questioning disposition, and a growing awareness of human nature and hypocrisy in the church, caused me to relinquish these beliefs with increasing fervor, until I became a self-declared born-again atheist. Still, I had not reflected on the psychology of religion.

About four years ago, some time after becoming a fully signed-up cryonicist, I began to experience the supernatural. I mean **really** experience it. Insights into the nature of god and man, the overwhelming feeling of having a religious mission, etc. Six weeks later I was in a police car speeding for the nearest psychiatric hospital. Other people were just not convinced that there was a Ship Of Glory bound for Antares hidden in the nearby mountains. They objected to my trying to expropriate their cars so that I could try to reach it.

Heavily drugged, diagnosed as schizophrenic, and surrounded by several Virgin Mary's, prophets of various descriptions, and spies, I had to make a choice--whether what I had gone through was real or not. The drugs helped me make that choice, which for me was lucky, but there was a lot of rebuilding to do.

Part of the rebuilding led to me thinking about what religion was, and where cryonics fitted into that emotional and intellectual package. The curious and hopeful thing was that cryonics did not form a part of the psychosis. I remember telling my mother in the comparatively early stages of my illness, as metaphysics was playing an increasing part in my thoughts, that I felt different, that I was dying inside somehow. When I was with people there was no link between my intellect and emotions—I didn't respond spontaneously to what people were saying, but instead analyzed each phrase for all its possible meanings, despite the context. My mother said that she thought I was changing as a result of recent experiences, and I was not to worry. Then, I suppose out of hope, she asked whether I would give up cryonics. "No", I said, "that's rational. It's not a part of all this."

A few minutes later I was hiding in my room. God and the Devil were looking for me. They were laughing sarcastically—time to dine on human flesh.

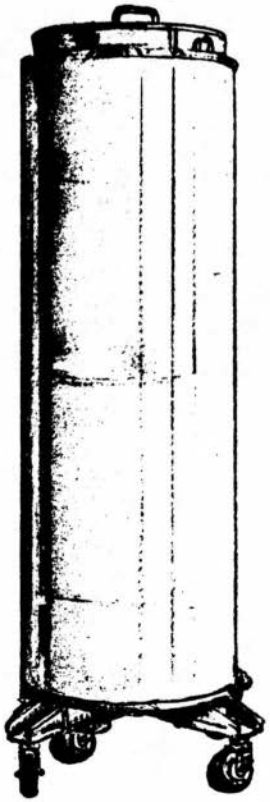
Most people's experience of religion seems to be like my early one. I have decided that these beliefs are somehow compartmentalized in the mind. If someone is seriously ill they are likely to say to themselves "Sure, I believe in Jesus, but I'll have the operation anyway. God helps those who help themselves." I can only conclude that the religious beliefs do not have anything to do with ordinary life, despite fervent claims to the contrary.

The true believers are the madmen. They **really** believe. They fast and

pray and give over all their worldly possessions. There is a continuum here with born-again evangelists at one end, and at the other the youth who stands, unnaturally still, mouth open praising god, and the Bible open to the book of Psalms. Many of our true believers are locked up—they believe so deeply in the supernatural that they cannot look after themselves. God will feed, clothe, and house them. (And he does, after a fashion.) What would 20 mg per day of Stelazine (an antipsychotic medication) do to a born-again Christian? I'd love to try the experiment!

And cryonics? Well, it's rational. It is no more a religion than the car I drive to work everyday or a real spaceship going to Antares. I suppose what I'm saying is that I don't "believe" in cryonics. Cryonics is not an article of faith any more than an automobile is. It is medical technology. I consider it a desirable attribute of human existence. Although cryonics is bound up with death and immortality, it is not a religion because we give effect to the idea by a concrete, realistic, and rational approach to the problem. We are acknowledging and dealing with the physical world.

Religious belief, however, manifests itself in activity which is secondary, and appears, in a causal sense, not to bear any relationship to the primary problem, which is death. Religious activities involve a lot of ritual, very similar to psychotic behavior, but carried out by a large number of people. (And these activities aren't even original!) In a frustrating attempt to work on the problem, religious belief becomes enmeshed with ethics, and right conduct becomes a means to eternal life.



None of this behavior makes rational sense. Thomas Szasz wrote "...only persons **conduct** themselves; animals behave, machines **function**, and stars **move**." I prefer to function—machines in good working order are intrinsically aesthetic.

Recently, and this is what prompted this article, I have heard several cryonicists talk about the possibility of registering cryonics as a religion for economic and legal reasons. Also there has been discussion of cryonics as a competing "meme" as an explanation of the generally heathen disposition of most cryonicists. It is wise to analyze the difference between religion and cryonics before making comparisons. There is cryonics as a religion and cryonics as technology. If we are to become a religion, even in a purely legal sense, we should be aware of what this label means. I consider it a dangerous label: belief should never replace directed and rational effort in cryonics.

CASE REPORT: NEUROPRESERVATION OF ALCOR PATIENT A-1068

By Michael G. Darwin, Jerry D. Leaf and Hugh Hixon

PART 1 OF 2

INTRODUCTION

On February 8th, 1985 ALCOR was notified that a Suspension Member with a long history of chronic illness was in critical condition at the University of Wisconsin Medical Center in Madison, Wisconsin. According to the patient's husband, physicians treating the patient expected deanimation to occur within a matter of hours or, at most, days.

A two-man rescue/stabilization team was dispatched to Madison to stand by in the event deanimation occurred. The team was equipped to undertake initial stabilization of the patient with a heart-lung resuscitator (HLR) and carry out total body washout (TBW) prior to transport.

On February 12th, 1985 the patient deanimated and was promptly coupled to an HLR and transported to a local mortuary where TBW was carried out. The patient was then shipped via airfreight to Cryovita Laboratories in Fullerton, California, for cryoprotective perfusion and cooling to liquid nitrogen temperature for long term care.

This report documents the care given this patient and seeks to critically evaluate the results of clinical and laboratory evaluations conducted during and after this suspension. From this evaluation, we hope to improve our techniques for cryonic care.

In keeping with established ethical practices and ALCOR's and Cryovita's own standards for confidential treatment of patient's records and identities, this patient will be referred to here only by her ALCOR number (A-1068).

PAST MEDICAL HISTORY

Past medical history and the admitting examination presented below are summarized from the patient's medical records provided by the hospital with permission of the patient and her next of kin.

The patient was a 68-year-old caucasian female with diffuse histocytic lymphoma whose history immediately prior to deanimation was one of ascites, abdominal pain, and elevated liver enzymes and bilirubin.

The patient had stage IV diffuse histocytic lymphoma since 1975. She was

initially treated with 5,000 rads of radiation to her spine for an epidural mass (which was surgically debulked) followed by systemic chemotherapy with Cyclophosphamide-Oncovin(vincristine)-Prednisone-Adriamycin(doxorubicin) (COPA) until 1977, at which time there was no evidence of disease. In March, 1984, she developed a malignant chylothorax and a mediastinal mass which biopsy disclosed to be diffuse histocytic lymphoma. She subsequently received chemotherapy with COPA and 3,500 rads to the mediastinum. This was followed by sclerosis of her left pleura with tetracycline in an attempt to control pleural fluid accumulation secondary to an obstructed thoracic duct. Her last chemotherapy was in October, 1984, with no evidence of disease at that time.

Three weeks prior to her final admission she developed weakness, abdominal distension, anorexia with weight loss, and light-colored stools. A work-up in Florida, where the patient was spending the winter, revealed elevated BUN, creatinine, alkaline phosphatase, SGOT, and bilirubin. Abdominal computerized tomography (CT) showed hepatomegaly with ascites, but without masses or adenopathy. Paracentesis revealed exudative fluid with suspicious cytology. Because of the likelihood that her disease had recurred, the patient and her husband elected to return to the University of Wisconsin Medical Center to pursue further medical care.

ADMITTING EXAMINATION

Past medical history was remarkable for hypothyroidism and a right lower extremity deep vein thrombosis. The admitting examination, from her medical records, describes a cachectic, chronically ill-appearing white female who was afebrile. Admitting blood pressure was 100/70. Examination of the head, eyes, ears, nose, and throat was remarkable for mild scleral icterus and palsy of the superior oblique muscle of the left eye. A CT scan of the head which was performed to rule out CNS neoplasm was unremarkable. The patient had no adenopathy on examination. Lungs were clear bilaterally. Cardiac examination revealed no jugular venous distension, S1 and S2 with a I/IV systolic murmur. The abdomen was distended, soft, and mildly and diffusely tender without rebound. The liver was 14 cm by percussion, with a firm, smooth, slightly tender edge. The patient had 2+ lower extremity edema. Neurologic examination was without focal findings except the left 6th cranial nerve findings noted above (palsy of the left superior oblique eye muscle).

HOSPITAL COURSE

Due to dehydration, as evidenced by her elevated BUN and creatinine, as well as by her hypercalcemia and hyperkalemia, the patient was vigorously supported with IV fluids and treated with Kayexalate™ for her hyperkalemia. This treatment resulted in improved renal function.

Due to the presence of ascites and deteriorating liver function, the patient underwent a laparoscopically-guided liver biopsy and paracentesis. This revealed grossly diffuse, massive replacement of the liver by lymphoma. Following the biopsy, the patient's course was complicated by a hypotensive episode and she required resuscitation with large amounts of fluid and temporary support of blood pressure with dopamine. The patient subsequently stabilized.

The patient's prognosis and situation were discussed with the patient and

her husband and it was decided that no cardiopulmonary resuscitation would be given prior to pronouncing legal death and that further care would consist of supportive and comfort measures only.

During the approximately 90 hours following her liver biopsy, the patient continued to require IV fluid support to maintain adequate blood pressure at a rate of approximately 400 cc per hour. Massive peripheral and systemic edema developed secondary to declining renal and liver function. Despite her continued downhill course, the patient remained alert and fully oriented until the evening of 2/11/85 when she began to experience dyspnea, followed by confusion, loss of consciousness, fall in blood pressure and subsequent respiratory and cardiac arrest. The immediate cause of deanimation was hypoxia secondary to massive pulmonary edema.

RESUSCITATION AND INITIAL STABILIZATION

The patient was pronounced legally dead on February 12, 1985 at 0248 hours CST (deanimation). Within approximately 3 minutes of the last agonal respiration, manual cardiac compression and bag-mask ventilation was begun. The patient was intubated and coupled to a Brunswick HLR 50-90. Following placement on HLR support, intravenous administration of transport medications was begun via Hickman catheter and the patient was packed in Zip-Loc plastic bags filled with finely crushed ice. The patient was afebrile at the time of deanimation with a measured rectal temperature of 36.5°C. Transport medications consisted of: 1.5 g sodium pentobarbital, 18 g tromethamine, 100 g mannitol, 7.5 mg verapamil, 2.0 mg naloxone, 4.4 mg metubine iodide, 210 mg cimetidine HCl, 375 mg methylprednisolone, and 500 ml Dextran 40 (10% in 5% dextrose solution). At the time of deanimation the patient was massively edematous with an estimated fluid load of 10 to 15 kg. Transport medications were administered on the basis of the patient's dry weight. All medications, excepting tromethamine and Dextran 40, were given as boluses while awaiting transport from the hospital. Sodium Pentobarbital was administered to secure anesthesia since the patient promptly exhibited return of agonal gasping and spontaneous movement in response to HLR support. Approximately 9 g of Tromethamine was given as a bolus and the other 9 g was administered over a 40-minute period. Dextran 40 was given by continuous IV drip over a 40-minute period.

INITIAL TRANSPORT

After initial stabilization on the HLR and administration of medications the patient was transported to a nearby mortuary for extracorporeal cooling and total body washout (TBW). Cardiopulmonary support and external cooling were continued en route. Upon arrival at the mortuary, the patient was transferred from the transport gurney to an embalming table and repacked in ice. HLR support was not interrupted as a result of the transfer operation. Immediately after positioning the patient on the table a blood sample was collected from an arterial line which was present in the right femoral artery. This and all subsequent samples were collected in 10 cc red stopper Vacutainers and refrigerated for later evaluation. Both discard and sample blood were noted to be bright red, indicating arterial oxygenation. Whole blood pH was measured immediately after sample collection with a Horizon model 5995 portable pH meter and was 7.25. Rectal temperature at 0432 hrs CST (deanimation + 1:44 hrs) was 27.5°C.

FEMORAL CANNULATION

The patient's right groin was prepared for surgery by swabbing with Betadine solution and draping with sterile towels and a fenestrated drape. The anatomical position of the right femoral artery and vein were located by reference to the pubic tubercle and the anterior superior iliac spine. An incision with a #10 scalpel blade was made at the midpoint between these two structures, beginning at the inguinal ligament and running parallel to the longitudinal axis of the leg for approximately 5 cm.

The femoral artery was promptly identified and an 18 fr. arterial cannula, USCI type 1860, introduced through an arteriotomy and secured with silk ties. Despite extensive dissection which consumed nearly an hour, the right femoral vein could not be located. It was later discovered from the patient's medical records (which were unavailable at the time of transport) that the patient had a history of thrombophlebitis with a venogram done in December, 1975 demonstrating extreme deep vein thrombosis of the right leg, including the entire right femoral vein.

Owing to lack of success identifying the right femoral vein, the left groin was prepared for surgery and the left femoral vein was promptly raised and cannulated with a 32 fr. venous cannula, USCI type 1967. After location of the left femoral vein, cardiopulmonary support was discontinued for approximately 10 minutes to control fluid accumulation and bleeding during cannulation. The patient's rectal temperature was 22°C at the time HLR support was interrupted. Both surgical procedures were complicated and greatly slowed by massive fluid accumulation in the wounds due to edema. These complications were particularly difficult to cope with in a field situation where no cautery, suction, or adequate surgical lighting was available.

At 0610 hrs CST (deanimation + 3:22 hrs) cannulation was complete and the patient was connected to a portable extracorporeal circuit consisting of a Sarns modular blood pump, a

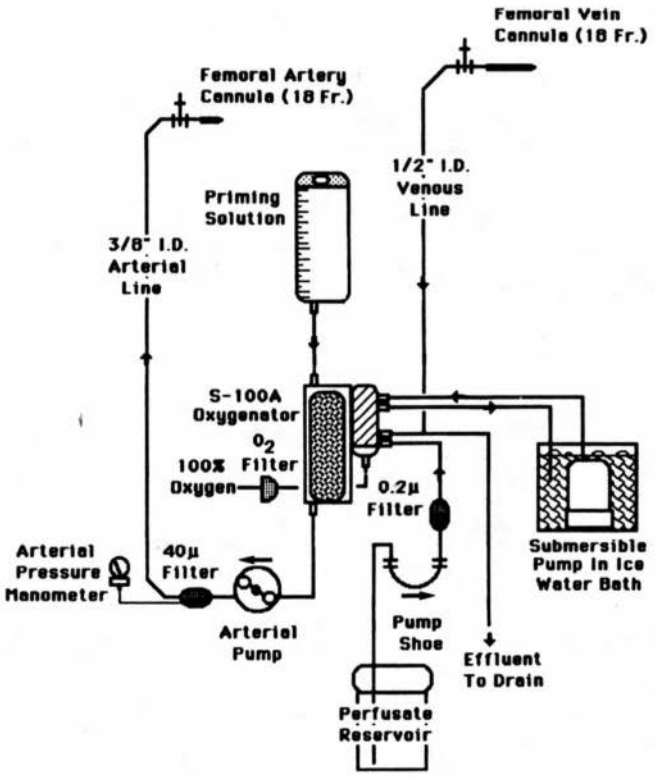


Figure 1. Portable Extracorporeal Circuit

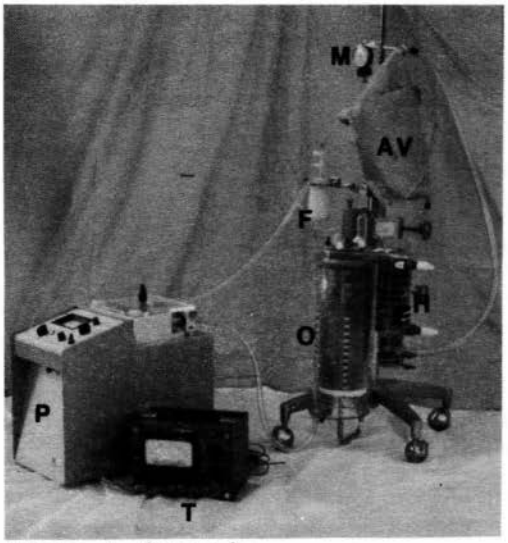


Plate 1 (Above).
Portable Extracorporeal Circuit

AV=Arterial and Venous lines in sterile package; F=Arterial filter (Shiley SF-20); H=Heat exchanger; M=Manometer; O=Oxygenator(Shiley S-100A); P=Sarns modular blood pump; T=Telethermometer

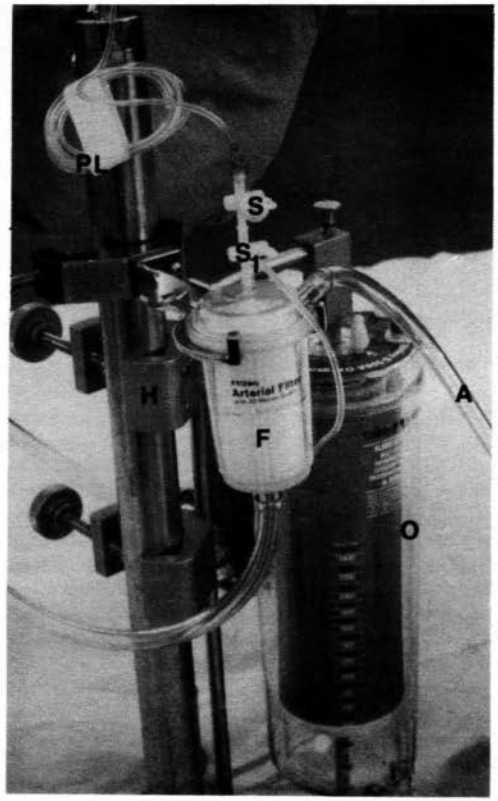


Plate 2. Portable Extracorporeal Circuit (Closeup)

A=Arterial line; F=Arterial filter (Shiley SF-20); H=Oxygenator holder clamp; O=Oxygenator(Shiley S-100A); PL=Pressure line to manometer; S=Stopcock to manometer pressure line; S1=Stopcock to arterial filter bleed line

Shiley S-100A bubble-type oxygenator and a Shiley SF-20, 20 micron filter (See Figure 1 and Plates 1 and 2). Perfusion pressure was measured at the Shiley SF-20 filter, anterior to the arterial cannula, employing an aneroid manometer with a sterile Tri-Med ISOLATER™ flexible membrane barrier to protect the aneroid from fluid contamination. A calibration curve of measured back pressure vs. measured flow had been generated in advance to account for the pressure increase resulting from cannula-induced flow restriction. This calibration curve was prepared using several cannulae in the size range appropriate for human femoral extracorporeal support.

The extracorporeal circuit was primed with 1,000 ml Dextran 40 in dextrose, 1,400 ml Plasmalyte, 50 ml 7.5% sodium bicarbonate, and 10,000 units of sodium heparin. Dextran 40 was selected to provide oncotic support in the prime due to its well-documented effects in inhibiting cold agglutination and improving microcirculation in hypothermia (Long, Sanchez, Varco, and Lillehei, (1961); Drake, Macalalad, and Lewis, (1961)). Extracorporeal blood cooling continued

at a blood flow rate of 3 liters/minute with a 6 liter/minute oxygen flow rate. Arterial pressure during blood recirculation was 92.5 mmHg. Blood cooling was terminated when the patient's rectal temperature was 12°C after approximately 20 minutes of perfusion. A blood sample from the arterial line was collected at 0610 hrs CST (deanimation + 3:22 hrs).

Following blood cooling, the patient was allowed to exsanguinate into the oxygenator and the blood collected in this fashion was discarded. The second pump shoe in the circuit was threaded into the pump and the oxygenator was filled with approximately 700 ml of mannitol-HEPES base perfusate (Table 1). Perfusate was sterilized "on line" by filtering into the oxygenator through a Pall 0.2 micron filter. Because the patient had massive interstitial edema and no ultrafiltration or hemodialysis equipment was available it was decided to raise the osmolality of the TBW perfusate from 320 mOsm to 450 mOsm by reducing the volume of water for injection added as diluent to the 4 liters of base perfusate concentrate. Since the TBW perfusion was to be carried out open circuit it was anticipated that the use of hyperosmolar/hyperoncotic perfusate would reduce the patient's fluid load by osmotically extracting water from the interstitial and intracellular spaces (Haupt and Rackow, (1982)).

Table 1.
Washout Perfusate Composition

Component	Concentration
Mannitol	226.5 mM
Glucose	13.3 mM
HEPES (Na^+ salt)	9.6 mM
Calcium chloride	1.3 mM
Magnesium chloride	2.7 mM
Potassium chloride	37.7 mM
Glutathione	6.7 mM
Adenine HCl	1.33 mM
Hydroxyethyl starch (Colloid Osmotic Pressure=29 mmHg, (Haupt and Rickow, 1982))	55 g/l
Heparin	1000 units/l

pH to 7.45 with potassium hydroxide
Osmolality: 450 mOsm

Following completion of the first "pass" of 700 ml, three more passes of base perfusate were perfused (open circuit) with a volume of 2,500 to 2,800 ml each at a temperature of 8°C. A perfusate (venous) effluent sample was collected at 0640 hrs CST (deanimation + 3:52 hrs) near the conclusion of TBW. The patient's temperature at the conclusion of perfusion was 8°C. The post-TBW hematocrit was unreadable (less than 1%). Examination of the patient following the conclusion of TBW revealed a marked decrease in edema as evidenced by markedly reduced limb girth and reversal of skin turgor which was present prior to TBW. No rigor was evident in the limbs.

PREPARATION FOR AIR TRANSPORT

At the conclusion of perfusion, the right femoral arterial and left femoral venous cannula were left in place and connected with a 3/8"-1/2" adaptor. The surgical wounds were then closed around the cannula. The wounds were covered in sterile dressing and waterproof plastic adhesive drapes, and the patient was transferred from the embalming table to a metal shipping case containing a rubberized canvas body pouch which had a bed of crushed ice in Zip-Loc bags in the bottom. The patient was then completely covered with ice in Zip-Loc bags in the body pouch and the remaining free space in the shipping case was also filled

with ice bags. The shipping case was closed and placed inside a plywood shipping box for air transport to Ontario Airport in Southern California.

ARRIVAL AND PREPARATION OF THE PATIENT

At 2110 hrs PST (deanimation + 20:22 hrs) on February 12 the patient arrived at the perfusion facilities in Fullerton, California. The shipping case was opened and the patient's pharyngeal and deep tracheal temperature were measured (the latter by placement of a probe via the endotracheal tube). At 2141 hrs PST (deanimation + 20:53 hrs) the pharyngeal temperature was 1.5°C and the tracheal temperature was 3.2°C. An initial examination of the patient conducted at that time disclosed the presence of rigor in the jaws and forearms, its absence in the neck and biceps and the presence of moderate rigor in both lower extremities.

At 2247 hrs PST (deanimation + 21:59 hrs) the patient was positioned on the operating table and the chest, neck, and scalp were prepared for surgery and sterile surgical drapes placed as previously described (Leaf, Federowicz, and Hixon, (1985b)) (Plate 3). At this time a temperature probe was placed in the left choana to more accurately monitor brain temperature. A venous perfusate sample drawn prior to the start of perfusion had a pH of 6.92. At 2336 hrs PST (deanimation + 22:48 hrs) a median sternotomy was begun.

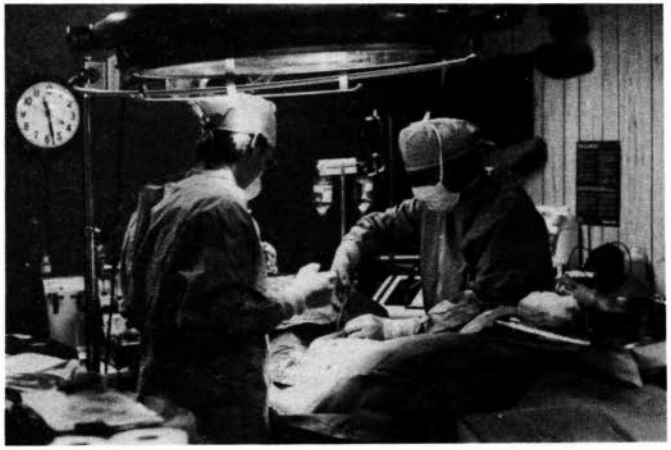


Plate 3. Preparation for Medial Sternotomy

SURGICAL PROTOCOL FOR CRYOPROTECTIVE PERFUSION

The basic surgical technique for circulatory access was similar to that employed in previous whole body cryonic suspensions (Leaf, (1981); Leaf and Quaife, (1981)). However, a new surgical approach was employed for vascular isolation of the head for neurosuspension (Fig. 2). In the past, vascular access for cryoprotective perfusion of neuropatients was achieved via bilateral cannulation of the internal carotid arteries. This approach necessitated open circuit perfusion of the head due to contamination of venous effluent with blood and loss of perfusate from the vertebral arteries, which are joined to the

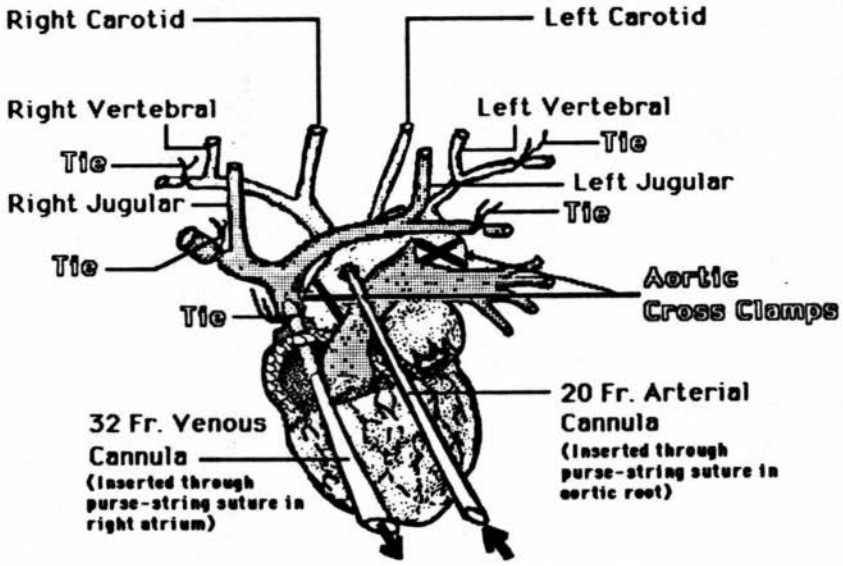


Figure 2. Vascular Isolation for Neuropreservation

carotid circulation via the Circle of Willis. A serious disadvantage of the carotid approach is the possibility of reduced or inadequate cerebral perfusion due to preferential loss of perfusate by retrograde flow through the vertebral arteries. Another potential problem with this approach, particularly in the elderly, is inadequate or absent cerebral perfusion as a result of carotid artery stenosis or thrombosis. A surgical approach which allowed utilization of all four cerebral arteries, i.e., both carotids and both vertebrals, would be more desirable.

In order to achieve such a four point cerebral perfusion the following approach was taken. The sternum was divided medially and a retractor was used to expose the heart. Figure 2 and Plate 4 show the vascular isolation of the cephalic circulation and the position of the arterial and venous cannulae. The arterial cannula was placed in the ascending aorta and arterial perfusate was directed to the brain by ligation of the subclavian arteries with silk ties just

Plate 4. Cannulae Positions in Median Sternotomy
A=Arterial cannula (20 fr.); C=Aortic cross-clamps; R=Sternal retractor; V=Venous cannula (32 fr.)

distal to the vertebral arteries. An aortic cross-clamp was placed just above the aortic valve to exclude the coronary circulation. The descending aorta was freed from the pulmonary artery by blunt dissection with Metzenbaum scissors. A second aortic cross-clamp was then applied to the descending aorta just distal to the left subclavian artery in order to exclude any arterial circulation to the body. Two purse-string sutures were then placed in the aortic root, one for a 20 fr. arterial perfusion cannula, and the other for an arterial pressure catheter which was connected to a Statham P23Db pressure transducer.

The pericardium was opened to expose the right atrium. A purse-string suture was placed in the apex of the right atrium and a 32 fr. venous cannula, USCI type 1967, was advanced through the atriotomy into the superior vena cava. Umbilical tape was passed around the superior vena cava and tied below the cannula tip. In order to prevent contamination of the recirculating system with venous circulation from the extremities, silk ties were placed on the left and right innominate veins just distal to the left and right internal jugular veins. Venous return was collected from a single cannula in the superior vena cava. This approach allowed closed-circuit perfusion of all four cerebral vessels and a gradual addition of glycerol without contamination of the perfusate with systemic blood or perfusate. An additional advantage of this technique was a 50% reduction in cannula cost since only one arterial and one venous cannula were required with this approach.

EXTRACORPOREAL CIRCUIT FOR CRYOPROTECTIVE PERFUSION

The extracorporeal circuit for cryoprotective perfusion is shown in Figure 3. The circuit consisted of two parts: a recirculating system to which the patient was connected and a glycerol addition system (Plate 5). The recirculating system was composed of a sterile 20 liter mixing/recirculating reservoir, arterial (recirculating) pump, an Erika HPF-200 hemodialyzer which was used as a hollow fiber oxygenator (Leaf and Federowicz, (1983)) a Sarns Torpedo heat exchanger, and a Pall EC1440 40 micron blood filter. The mixing reservoir was continuously stirred with a 2" teflon-coated magnetic stirring bar and a Thermolyne type 7200 magnetic stirrer. Glycerol concentrate was continuously added to the recirculating system with a Travenol 5M1153 hemodialysis pump. Glycerol concentrate was sterilized in line with a Pall PP3802 0.20 micron pre-bypass filter as it was delivered to the recirculating system. The circuit was cut and assembled at the time of use using presterilized lengths of tubing and other components.

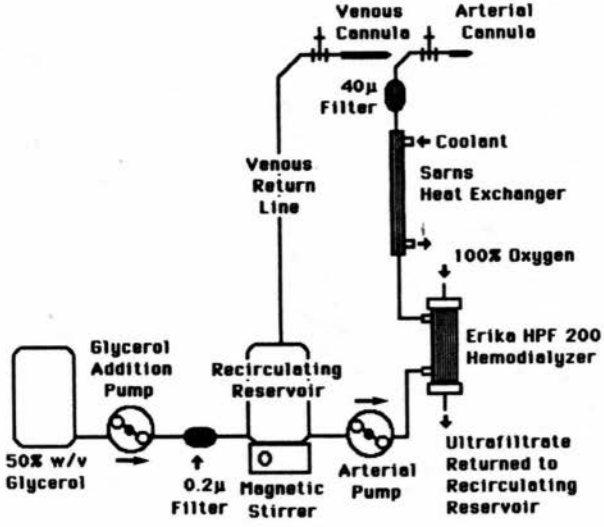
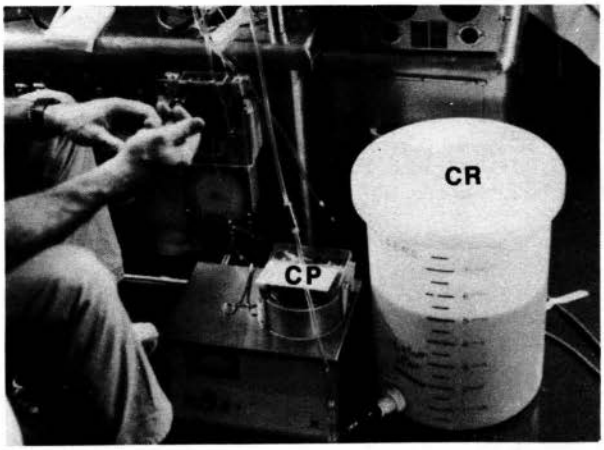


Figure 3. Extracorporeal Circuit for Cryoprotective Perfusion

Plate 5. Pump Rate Check on Glycerol Addition System

CP=Cryoprotectant pump;
CR=Glycerol concentrate reservoir



Cultures of the recirculating 5% glycerol perfusate which were taken before the patient was connected to the circuit revealed the presence of a few colonies of the gram negative microorganism Acinetobacter Calcoaecitus Biotype LWOFF1 (commonly know as Mima Polymorpha). This organism is ubiquitous and is found in the soil, on human skin, and on environmental surfaces. The presence of this organism in the perfusate prior to perfusion is indicative of a break in sterile technique either during assembly of the perfusion circuit or collection of the perfusate sample for culture. In the future, preassembled circuits will be used to minimize the chance of bacterial contamination of this kind.

PERFUSATE PREPARATION

Cryoprotective perfusion was begun at 0216 hrs PST (deanimation + 25:28 hrs) on 2/13/85 using 14 liters of 5% w/v glycerol in a mannitol-HEPES base perfusate. Later laboratory evaluation of this perfusate, carried out as part of ALCOR's quality control operations, revealed that a potentially serious error had been made during perfusate preparation. Personnel preparing the perfusate failed to follow established procedure which calls for the use of a check list to insure addition of all ingredients in the right quantities and appropriate adjustment of pH and osmolality. Failure to use the check list resulted in the omission of calcium chloride and magnesium chloride from the perfusate (these ingredients must be added as a solution which in turn must be prepared immediately prior to use; thus they are not kept with the powdered perfusate components). The composition of the base perfusate as it was prepared and administered is given in Table 2.

Table 2. Perfusate Composition

Component	Concentration
Mannitol	170 mM
Glucose	10 mM
HEPES (Na^+ salt)	7.2 mM
Potassium chloride	28.3 mM
Glutathione	5.0 mM
Adenine HCl	1.0 mM
Hydroxyethyl starch (Colloid Osmotic Pressure=29 mmHg, Haupt and Rickow, 1982))	55 g/l
Heparin	1000 units/l

pH to 7.72 with potassium hydroxide
Osmolality: 315 mOsm

Perfusion with solutions containing less than 50 uM calcium results in loss of calcium from cell membranes, which causes massive edema due to cellular swelling. (Zimmerman, et al, 1967). Fortunately, as later laboratory analysis of effluent samples and recirculating perfusate disclosed, adequate calcium and magnesium were present in the perfusate as a result of their presence as normal impurities in the hydroxyethyl starch employed as a colloid in the perfusate. HES samples from the same lot employed on this suspension have been tested and shown to contain 0.50 mM Ca^{++} in 6% solutions. The measured arterial perfusate calcium by ionization averaged 0.46 mM, and venous perfusate showed an average of 0.48 mM, which are well above the 50 uM danger level. The perfusate contained 5.5% HES, which correlates well with these arterial and venous ionized calcium values.

PERFUSION CONDITIONS

Arterial perfusate temperature averaged 13.0 $\pm$ 1°C and a flow rate of 500 cc/min was maintained throughout perfusion. Arterial perfusion pressure was 30-50 mmHg. Patient tracheal, sinus, and frontal brain temperature during the course of perfusion and cephalic isolation are shown in Figure 4.

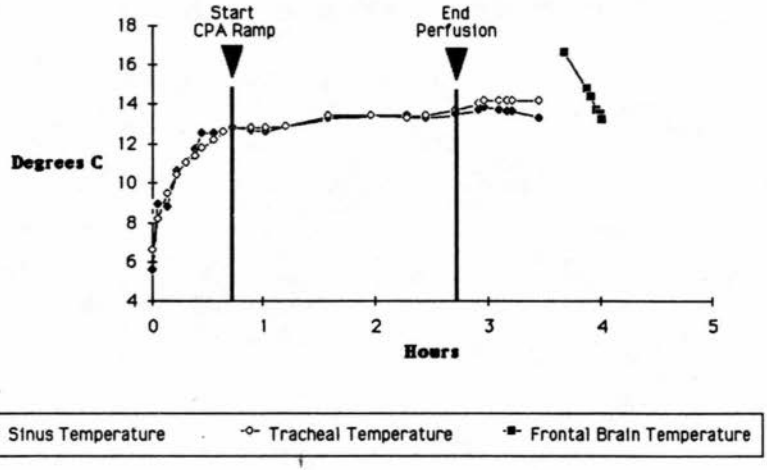


Figure 4. Temperatures During Perfusion

Paired arterial and venous samples were drawn at 15 minute intervals during perfusion for determination of pH and glycerol concentration, and for later evaluation of electrolytes and other chemistries. Arterial and venous pH during perfusion are shown in Figure 5. The venous pH was persistently lower than the arterial. Despite oxygenation and perfusate flow rates far above those achieved in the past (Leaf, Federowicz, and Hixon, (1985b)) acidosis remained a problem. As in recent suspensions (Leaf, Federowicz, and Hixon, (1985b)), it was thought that the venous pH remaining persistently below the arterial pH was probably indicative of active anerobic metabolism, and it was expected that oxygenation would correct this problem. However, the problem persisted despite oxygenation.

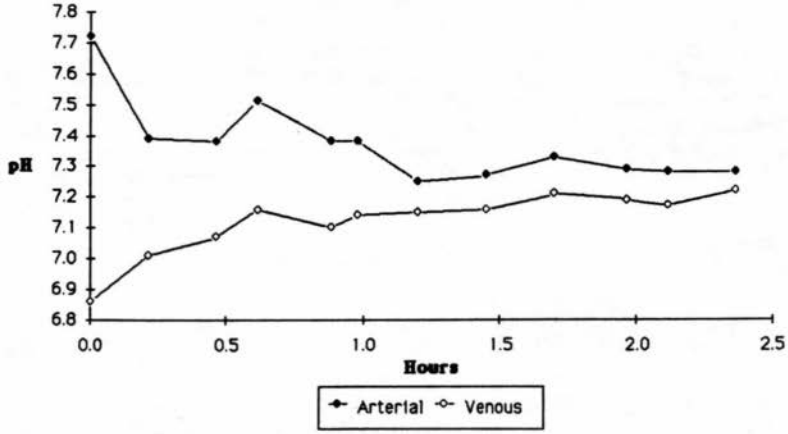


Figure 5. pH During Perfusion

The acidosis experienced by this patient may in part be due to inadequate levels of HEPES in the perfusate. Foreman et al have demonstrated good control of pH during hypothermic organ perfusion employing HEPES as the buffer at approximately twice the concentration used on this patient (Foreman, Pegg, and Armitage, (1985)). Evaluation of increasing the buffer concentration, use of another buffer with a higher pK, or active electronic control of pH is needed in an animal model in an attempt to solve this problem.

Corneal flattening was present as a normal post-TBW/postdeanimation change prior to the start of perfusion and became more pronounced, proceeding to frank ocular flaccidity after the first 15 minutes of perfusion. During the last 20 minutes of perfusion ocular volume rebounded to preperfusion levels and immediately prior to the termination of perfusion the eyes were firm and the corneas were undimpled, probably reflecting intraocular fluid accumulation and/or edema.

CRYOPROTECTANT ADDITION

Four liters of the 5% w/v perfusate were flushed open circuit through the patient's cephalic circulation and discarded, after which the circuit was closed and recirculation was begun at a flow rate of 500 cc/min. After 28 minutes of recirculation, 6 liters of perfusate were drained from the circuit, discarded, and replaced with 6 liters of fresh 5% w/v glycerol-containing perfusate. At 0259 hrs PST (deanimation + 26:11 hrs), 7 liters were drained from the perfusate reservoir and replaced with fresh 5% glycerol perfusate.

Linear, gradual addition of glycerol to the recirculating system was begun at 0300 hrs PST (deanimation + 26:12 hrs) with a precalibrated pump, using a 50% w/v glycerol solution in mannitol-HEPES base perfusate (also prepared without calcium chloride or magnesium chloride). Electrolyte and other solute concentrations were kept constant on a molar basis at all glycerol concentrations. The rate of addition of glycerol to the recirculating system was calculated prior to initiation of cryoprotective perfusion by estimating the

fluid load represented by the patient's head and adding that to the known volume of the extracorporeal circuit. A relatively large volume recirculating reservoir (as contrasted with past suspensions) was used to minimize the effects of errors in estimating the patient's fluid contribution, i.e., to act as an osmotic buffer during glycerolization.

Previous animal studies carried out by ALCOR and Cryovita have demonstrated a serious problem with very stable stratification or "layering" of cryoprotective concentrate as it is introduced into the recirculating system. To avoid this problem, the recirculating or "mixing" reservoir was continuously stirred using a bar-type magnetic stirrer as described above.

The progress of glycerolization was monitored by osmometry (Precision Systems MicroOsmette Model 5004 freezing point osmometer) to provide, where necessary, corrective negative feedback to the calculated ramp.

A terminal venous perfusate glycerol concentration of 3.0 M was sought with an additional objective that arterial/venous (A/V) glycerol concentration difference be held to less than 100 mM throughout perfusion. Glycerol concentration over the course of cryoprotective perfusion is shown in Figure 6. The objective of maintaining the A/V glycerol difference to 100 mM or less was achieved throughout most of the perfusion. Unfortunately, due to the development of edema perfusion had to be terminated before the target 3.0 M glycerol concentration was reached in the venous perfusate.

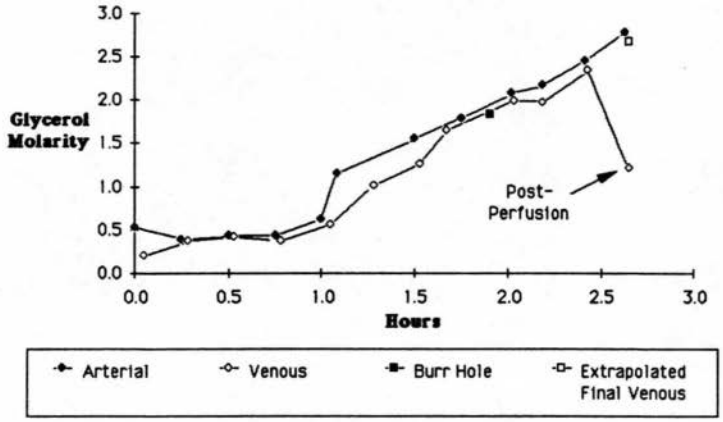


Figure 6. Glycerol Concentration During Perfusion

Cryoprotective perfusion lasted for 158 minutes. Perfusion was terminated at 0454 hrs PST (deanimation + 28:06 hrs) as a result of cerebral edema. Venous glycerol concentration (extrapolated) at the conclusion of perfusion was approximately 2.8 M.

TREPHINATION

After cryoprotective perfusion was begun, an incision was made in the scalp over the left parietal lobe. A burr hole was made as previously described (Leaf, Federowicz, and Hixon, (1985b)) (Plates 6 and 7) to observe changes in cerebral cortical volume and evaluate the degree of blood washout achieved during prior TBW perfusion. The cortical surface was visualized at approximately 0315 hrs (deanimation + 26:27 hrs). Since the burr hole was not made until after the start of cryoprotective perfusion it was not possible to

evaluate the degree of cerebral volume reduction (dehydration) the patient experienced during the start of glycerolization. At the time the cerebral cortex was first visualized it appeared normal in volume and free of any blood-filled vessels (Plate 8).

Near the conclusion of perfusion the burr hole began to leak clear fluid. Perfusion pressure remained constant and it was felt that this leakage represented weeping of fluid from the cortical surface, the meninges, the dura, or all three, rather than rupture of a cerebral vessel. This phenomenon has been observed primarily in ischemically injured cats, and to a lesser degree in nonischemic cats being glycerolized to 3.0 M (Federowicz and Leaf, (1983)). In the cat, the development of such burr hole drainage is closely correlated with rapid progression of cerebral edema and is usually not observed until after a venous glycerol concentration of 2.0 M or greater has been reached.

Within 20 minutes after significant drainage from the burr hole was first noted, cerebral edema had developed to the point that the cortical surface was beginning to bulge against the margins of the burr hole. If perfusion was temporarily discontinued, the cortical surface subsided to several millimeters below the margin of the burr hole. Conceivably, despite the development of cerebral edema, perfusion might have been continued in an "on-off" mode. However, due to the increasing rate of leakage of fluid from the burr hole it was decided to terminate perfusion. The flow rate of fluid from the burr hole near the end of perfusion was in excess of 5 cc/min.

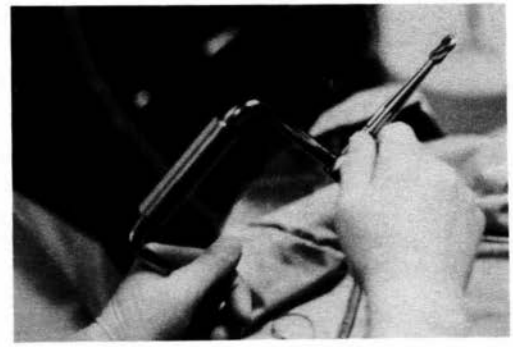


Plate 6. Hudson Cranial Drill With 9mm Burr Used to Open Hole in Calvarium

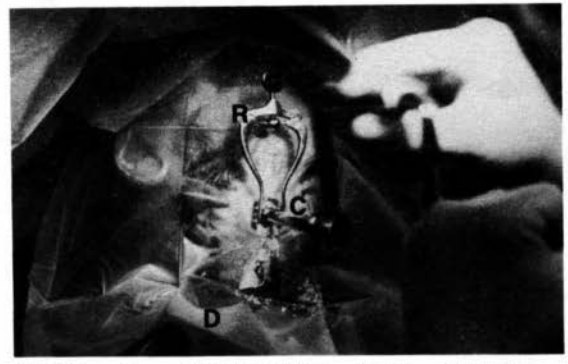


Plate 7. Trephanation With Hudson Cranial Drill

C=Cranial drill; D=Self-adhesive sterile drape; R=Weitlaner self-retaining retractor

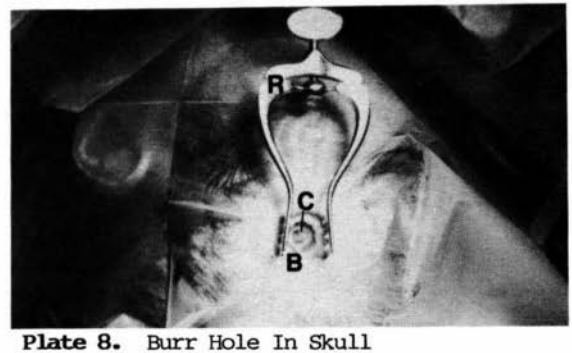


Plate 8. Burr Hole In Skull

B=Burr hole; C=Cerebral cortical surface; R= Weitlaner retractor

After the conclusion of perfusion the stainless steel disc of a YSI Type 729 implantable thermistor probe was placed on the surface of the brain, and the burr hole was filled with bone wax. The wound was then closed using interrupted 2-0 Tycron suture and the probe anchored as previously described (Leaf, Federowicz, and Hixon, (1985b)) (Plate 9).

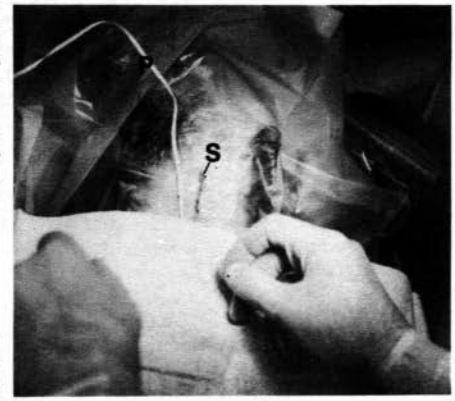


Plate 9. Burr Hole Closure
P=Probe Lead Wire; S=Suture line

GROSS EFFECTS OF GLYCEROLIZATION

Despite the development of interstitial edema, cellular dehydration of the skin and other structures of the head and neck was very evident, even at the conclusion of perfusion. Within 3 to 5 minutes of the start of perfusion the skin of the patient's face and neck developed the translucent, amber mottling typical of human glycerol perfusions (Federowicz, (1973)). Marked facial dehydration developed as the glycerol concentration was further increased. Efforts to minimize or eliminate these effects by carrying out glycerolization at 13°C to 14°C as opposed to 6°C to 8°C as has been done in the past (Leaf, Federowicz, and Hixon, (1985b)) were unsuccessful.

One interesting feature of this dehydration was the development of a very sharp line of demarcation between the perfused and unperfused areas of the patient's skin. At the conclusion of perfusion the zone between amber, perfused skin, and normal appearing unperfused skin was as sharp as if it had been scribed with a pen. This is evidence of the effectiveness of the vascular isolation techniques employed on this patient in confining perfusion to the cephalic circulation.

END OF PART 1

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FEBRUARY-MARCH 1986 MEETING CALENDAR

ALCOR meetings are usually held on the first Sunday of the month. Guests are welcome. Unless otherwise noted, meetings start at 1:00 PM. For meeting directions, or if you get lost, call ALCOR at (714) 738-5569 and page the technician on call.

ALCOR

ALCOR LIFE EXTENSION FOUNDATION

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FULLERTON, CALIFORNIA 92635
(714) 738-5569

The FEBRUARY meeting will be at the home of:

(SUN, 2 FEB 1986) Allen Lopp
13354 Veracruz St.
Cerritos, CA

DIRECTIONS: Take the Artesia Freeway (State 91) to Cerritos (Between the San Gabriel Freeway (I-605) and the Santa Ana Freeway (I-5)), and get off at Carmenita Road going north. Veracruz is the third street on the left after 183rd St. 13354 is on the southwest corner of Carmenita and Veracruz. Park in the lot of the Thrifty Drugstore directly across the street.

The MARCH meeting will be at the home of:

(SUN, 9 MAR 1985) Mike Darwin and Scott Greene
(SECOND SUNDAY) 350 W. Imperial Highway, #21
Brea, CA

DIRECTIONS: Take the Orange Freeway (Hwy 57) to Imperial Highway (Hwy 90), and go west through Brea on Imperial Highway. 350 is about one mile from the freeway, and in the third block beyond Brea Blvd., on the south (left) side. If the gate is closed, park on the streets north of Imperial. Be careful crossing Imperial. There is a blind curve to the east and a blind hill to the west at this point.

The APRIL meeting will be at the home of:

(SUN, 6 APR 1985) Sherry Cosgrove
3100 Palm Drive, #1
Fullerton, CA

DIRECTIONS: Take the Orange Freeway (Hwy 57) to Yorba Linda Blvd., just north of the CSU Fullerton campus. Go east on Yorba Linda to the second stop light (Placentia Ave.). Go north (left) on Placentia, around to Palm Drive. Turn right on Palm. 3100 is an apartment block immediately on the right, behind the K-Mart parking lot, and is not numbered. #1 is at the corner of the street and the parking lot.

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